REMARKS/ARGUMENTS

The foregoing amendments in the specification and claims are of a formal nature, and do not add new matter.

Prior to the present amendment, Claims 28-47 were pending in this application and were rejected on various grounds. With this amendment, Claims 28-32, 34-37 and 41-43 have been canceled without prejudice, Claims 33, 38-39 and 44 have been amended, and new Claims 48-54 have been added.

Claims 33, 38-40 and 44-54 are pending after entry of the instant amendment. Applicants expressly reserve the right to pursue any canceled matter in subsequent continuation, divisional or continuation-in-part applications.

The amendments to the specification and claims are fully supported by the specification and claims as originally filed and do not constitute new matter. In addition, new Claims 48-54 are fully supported by the specification as originally filed. Support for new Claims 48-54 can be found at least on page 155, lines 13-16, on page 282, lines 12-19 and on page 308, line 38 to page 309, line 7 of the specification.

Specification

The specification has been amended to remove embedded hyperlink and/or other form of browser-executable code. Further, Applicants have amended the specification to comply with the provisions of the Budapest Treaty.

Priority

The Examiner states that given the huge list of parent applications, the present application is given no benefit of the priority to any of the provisional applications.

The Examiner's attention is respectfully directed to the Preliminary Amendment filed on August 29, 2002, which states that the present application is "a continuation of, and claims priority under 35 U.S.C. §120 to, U.S. Application No. 09/946,374, filed February 18, 2000, which claims priority under 35 U.S.C. §119 to U.S. Provisional Application No. 60/162,506,

filed October 29, 1999, where PCT/US00/04342 is a continuation-in-part of, and claims priority under 35 U.S.C. §120 to, U.S. Patent Application No. 09/403,297, now abandoned, which is the National Stage filed under 35 U.S.C. §371 of PCT Application No. PCT/US99/20111, filed September 1, 1999, which claims priority under 35 U.S.C. §119 to U.S. Provisional Application No. 60/100,661, filed September 16, 1998."

Applicants rely on the gene amplification assay (Example 143) for patentable utility which was first disclosed in U.S. Provisional Application No. 60/162,506, filed October 29, 1999, priority to which has been claimed in this application. All claim limitations are fully supported by the disclosure of U.S. Provisional Application No. 60/162,506, filed on October 29, 1999, which is specific for the PRO1269 polypeptide and its coding sequence.

Further, the PRO1269 polypeptide sequence and its encoding nucleic acid sequence were first disclosed in the U.S. Provisional Application No. 60/100,661, filed on September 16, 1998, priority to which has been claimed in this application.

Claim Rejections – 35 U.S.C. §112, First Paragraph

Claims 28-37 and 41-47 were rejected under 35 U.S.C. §112, first paragraph, because, according to the rejection, the specification, "while being enabling for the specific PRO1269 sequence of SEQ ID NO:215, does not reasonably provide enablement for anything which encodes SEQ ID NO: 216, which hybridizes to SEQ ID NO: 215 or which shares some percent identity." The Examiner further asserts that the specification, "while showing PRO1269 could be generically used in a variety of ways, provides no guidance on the actual use or relevance of PRO1269. The reference to the related bacterial protein, granulocyte A peptide family, fails to provide any utility since there is no evidence that PRO1269 shares any functional relationship with this protein."

Without acquiescing to the Examiner's position in the current rejections, and without prejudice to further prosecution of the subject-matter in one or more continuation or divisional applications, Claims 28-32, 34-37 and 41-43 have been canceled. Applicants respectfully submit that the cancellation of Claims 28-32, 34-37 and 41-43 renders the rejection of these claims

moot. Further, Claim 33, as amended, no longer recites a nucleotide acid sequence encoding the polypeptide of SEQ ID NO: 216.

Example 143 of the present application describes in detail the isolation of genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 8, including primary lung cancers of the type and stage indicated in Table 7. As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control. Gene amplification was monitored using real-time quantitative TaqMan PCR. Table 8 shows the resulting gene amplification data. Further, Example 143 explains that the results of TaqMan™ PCR are reported in ΔCt units, wherein one unit corresponds to one PCR cycle or approximately a 2-fold amplification relative to control, two units correspond to 4-fold amplification, 3 units to 8-fold amplification etc. PRO1269 showed approximately 1.14-1.26 ΔCt units which corresponds to $2^{1.14}$-$2^{1.26}$- fold amplification or 2.204 fold to 2.395-fold amplification in lung tumors.

Applicants respectfully submit that based on the teachings of Example 143 and the general knowledge available in the art at the priority date of the invention, one skilled in the art would be able to practice the claimed invention in its full scope without any undue experimentation. Applicants respectfully submit, and as the Examiner noted, that the level of skill in this field is relatively high, and is represented by a Ph.D. scientist having several years of experience in the pertinent field. Accordingly, the teaching imparted in the specification must be evaluated through the eyes of a highly skilled artisan as of the date the invention was made. As the M.P.E.P. states, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation" *In re Certain Limited-charge cell Culture Microcarriers, 221 USPQ 1165, 1174* (Int'l Trade Comm'n 1983), *aff'. sub nom., Massachusetts Institute of Technology v A.B. Fortia,* 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985) M.P.E.P. 2164.01.

Further, based on the instant disclosure, which details how to make and use the claimed nucleic acids and the advanced knowledge in the art at the time of filing, one skilled in the art

would know exactly how to make and use the claimed nucleic acids for the diagnosis of lung cancer; for example, by using diagnostic methods based on hybridization to such amplified sequences.

Accordingly, Applicants respectfully request the Examiner to reconsider and withdraw the rejection of Claims 33, 38-40 and 44-47 under 35 U.S.C. §112, first paragraph.

Claim Rejections – 35 U.S.C. §112, First Paragraph (Written Description)

Claims 28-37 and 41-47 have been rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The Examiner further asserts that members of the claimed genus were not unified by any structural features or limitations, and, because the claimed genus was highly variant, the written description requirement of the patent statute was not met.

Without acquiescing to the Examiner's position in the current rejections, and without prejudice to further prosecution of the subject-matter in one or more continuation or divisional applications, Claims 28-32, 34-37 and 41-43 have been canceled. Applicants respectfully submit that the cancellation of Claims 28-32, 36-37 and 41-43 renders the rejection of these claims moot.

The Examiner is therefore respectfully requested to reconsider and withdraw the rejection of Claims 33 and 44-47 for allegedly lacking written support.

Claim Rejections - 35 U.S.C. §102

Claims 28-47 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by Young *et al.*, (U.S. Patent No. 6,444,790, effective priority date December 23, 1998).

Applicants respectfully submit that the cancellation of Claims 28-32, 34-37 and 41-43 renders the rejection of these claims moot.

Applicants have claimed priority to U.S. Provisional Application No. 60/100,661, filed on September 16, 1998. The present application is entitled to the priority date of September 16, 1998, which precedes, at least by three months, the earliest priority date of Young *et al.* (December 23, 1998). Accordingly, Young *et al.* is not prior art against the present application and Claims 33, 37-40 and 44-47 are patentable.

Further, Applicants respectfully submit the Declaration under 37 C.F.R. §1.131 by Dr. Botstein, Dr. Goddard, Dr. Godowski, Dr. Gurney, Ms. Roy, Mr. Watanabe and Dr. Wood that establishes that Applicants had cloned, sequenced and homology to granulocyte peptide A identified before the prior art date of December 23, 1998. The consideration of the Declaration is respectfully requested.

Applicants respectfully submit that an executed copy of the Declaration will be submitted to the Examiner shortly.

U.S. Provisional Application No. 60/100,661 simply needs to disclose what is disclosed in the cited reference to support the priority claim

Applicants respectfully submit that in order to overcome the 35 U.S.C. §102(e) rejection over Young *et al.,* the Declaration by Dr. Botstein, Dr. Goddard, Dr. Godowski, Dr. Gurney, Ms. Roy, Mr. Watanabe and Dr. Wood ("Declaration") simply needs to provide a disclosure commensurate in scope with the disclosure in the prior art document by Stahl to support the priority claim.

In order to remove a reference as a prior art, "[i]t is sufficient if [the affidavit under Patent Office Rule 131] shows that as much of the claimed invention as is taught in the reference has been reduced to practice by the [patentee] prior to the date of the reference." *In re* Stempel, 241 F.2d 755, 757 (1957). In *In re* Stempel, the patent applicant (Stempel) had claims directed to both (i) a particular genus of chemical compounds (the "generic" claim) and (ii) a single species of chemical compound that was encompassed within that genus (the "species" claim). In support of a rejection under 35 U.S.C. §102, the examiner cited against the application a prior art reference that disclosed the exact chemical compound recited in the "species" claim. In response to the rejection, the patent applicant filed a declaration under 37 C.F.R. §1.131 demonstrating

that he had made that specific chemical compound prior to the effective date of the cited prior art reference. The Court found the applicant's 37 C.F.R. § 1.131 declaration effective for swearing behind the cited reference for purposes of both the "species" claim and the "genus" claim. Specifically, the Court stated in support of its decision that "all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference." *Id.* at 759.

Furthermore, the Examiner is respectfully directed to *In re* Moore, 170 USPQ 260 (CCPA 1971), where the holding in *In re* Stempel was affirmed. In *In re* Moore, the patent applicant claimed a particular chemical compound in his patent application and the examiner cited against the applicant a prior art reference under 35 U.S.C. §102 rejection which disclosed the compound but did not disclose any specific utility for the compound. The patent applicant filed a declaration under 37 C.F.R. §1.131 demonstrating that he had made the claimed compound before the effective date of the cited prior art reference, even though he had not yet established a utility for that compound. On appeal, the Court indicated that the 131 declaration filed by the patent applicant was sufficient to remove the cited reference. The Court relied on the established "Stempel Doctrine" to support its decision, stating:

> An applicant need **not** be required to show [in a declaration under 37 C.F.R. § 1.131] any more acts with regard to the subject matter claimed that can be carried out by one of ordinary skill in the pertinent art following the description contained in the reference ... the determination of a practical utility when one is not obvious need **not** have been accomplished prior to the date of a reference unless the reference also teaches how to use the compound it describes.

In re Moore, 170 USPQ at 267 (emphasis added).

Thus, *In re* Moore confirmed the holding in *In re* Stempel which states that in order to effectively remove a cited reference with a declaration under 37 C.F.R. §1.131, an applicant need only show that portion of his or her claimed invention that appears in the cited reference.

Young *et al.* discloses a protein designated peptidoglycan recognition protein-related proteins-chondrosarcoma (PGRP-C), which is identical to the PRO1269 polypeptide of the present application. The specification discloses that PGRG-C has sequence homology with both

human peptidoglycan recognition protein (PGRP) and murine Tag-7 as support for the sequence possibly being useful in augmenting the immune system in areas such as immune recognition and immune system activation. (See U.S. Patent No. 6,444,790, column 1 lines 16-21; column 3, lines 38-46; column 60, lines 56-67; column 61, lines 15-53). However, the specification of the issued U.S. patent is devoid of any experimental data demonstrating the biological activity of PGRP-C, or identifying any specific diseases associated with the expression level of this protein or its encoding gene.

Accordingly, since the cited reference by Young only discloses a polynucleotide sequence, its encoding nucleic acid sequence and a sequence homology, Applicants respectfully submit that the Declaration simply needs to show possession of the polypeptide sequence, its encoding polynucleotide sequence as disclosed in Young, and a sequence homology in order to overcome the 35 U.S.C. §102 rejection.

Applicants respectfully submit that U.S. Provisional Application No. 60/100,661, filed on September 16, 1998, provides the nucleic acid and amino acid sequences of the PRO1269 polypeptide and the homology of the polypeptide to the bovine granulocyte peptide A precursor (see U.S. Provisional Application No. 60/100,661 on page 15, under the section titled "Full-length PRO1269"). Considering its homology to the granulocyte peptide A, Applicants further suggest the PRO1269 polypeptide to be newly identified member of the granulocyte A peptide family and may possess biological activity typical of that family of peptides.

The Declaration clearly states that U.S. Provisional Application No. 60/100,661, filed on September 16, 1998, discloses sequences designated as SEQ ID NO:2 and SEQ ID NO:1, which are identical to SEQ ID NO:215 and SEQ ID NO:216, respectively, of the above-identified application. Further, the Declaration confirms that U.S. Provisional Application No. 60/100,661, filed on September 16, 1998, discloses that SEQ ID NO:1, corresponding to SEQ ID NO: 216 of the above-identified application, has homology to granulocyte peptide A.

Accordingly, Applicants respectfully submit that the disclosures are commensurate in scope and that U.S. Provisional Application No. 60/100,661, filed on September 16, 1998, discloses all that the cited prior art discloses.

Consequently, based on the holdings of *In re* Stempel and *In re* Moore, Applicants respectfully submit that Young *et al.* is not prior art under 102(e) since its effective priority date is after the invention by the Applicants for patent. Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of Claims 33, 38-40 and 44-47 under 35 U.S.C. §102(e).

CONCLUSION

In conclusion, the present application is believed to be in *prima facie* condition for allowance, and an early action to that effect is respectfully solicited. Should there be any further issues outstanding, the Examiner is invited to contact the undersigned attorney at the telephone number shown below. Please charge any additional fees, including fees for additional extension of time, or credit overpayment to Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-2830 P1C53**). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: October 18, 2004

By: _____
Ginger R. Dreger (Reg. No. 33,055)

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